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## **The role of inhibition in motor performance and learning**

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**Introduction:** Understanding the neurophysiological underpinnings of motor plasticity is of prime importance, not least for developing novel therapeutic approaches after a stroke. There is substantial evidence from animal models to support the hypothesis that modulation of GABA, the major inhibitory neurotransmitter, is a necessary step in motor learning. However, until recently it has been difficult to assess whether GABA is necessary for plasticity *in vivo* in humans.

**Methods:** Recently, we have developed multimodal neuroimaging and brain stimulation approaches to investigate the role of GABA in motor plasticity. Here, I will describe recent advances in our work using Magnetic Resonance Spectroscopy (MRS), often in combination with transcranial direct current stimulation (tDCS) or transcranial alternating current stimulation (tACS), to study motor plasticity.

**Results:** The key findings from our newest studies can be summarised as follows:

1. Local GABA levels control local cortical functional organisation, as determined by high-resolution fMRI, and predict behaviour.
2. Local GABA levels are decreased during motor learning, in a manner related to learning of that task.
3. tDCS to left M1 leads to significant modulation of the inter-hemispheric GABA balance, such that the magnitude of GABA changes in the non-stimulated M1 are related to structural connectivity between the two cortices.

**Discussion:** These results suggest that MRS-assessed GABA is a functionally-relevant measure of local inhibition and is modulated during plasticity induction: changes in local levels of inhibition relate to local performance and changes within the wider functional network are determined by structural connectivity within that network. These results therefore start to shed light on network-level changes in inhibition and pave the way for a new understanding of the mechanisms underpinning motor recovery after stroke, where recruitment of multiple motor areas is key to recovery.

Keywords: tDCS, MR Spectroscopy, Motor Learning, GABA